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EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
10/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,105	ISHII ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,17,18,21,24,25,28,29,31,32,37-40,42,43,46 and 47* is/are pending in the application.

4a) Of the above claim(s) *1-3,10,11,14,21,24,28,29,31,32,37-40,42,46 and 47* is/are withdrawn from consideration.

5)☒ Claim(s) *7* is/are allowed.

6)☒ Claim(s) *4,5,8,9,12,13,17,18,25 and 43* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7//72008* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment and Arguments

The Amendment filed on 7/7/2008 in response to the previous Non-Final Office Action (2/7/2008) is acknowledged and has been entered.

Claims 15-16, 19-20, 22-23, 26-27, 30, 33-36, 41, 44-45, are 48-50 are cancelled.

Claims 1-14, 17-18, 21, 24-25, 28-29, 31-32, 37-40, 42-43, 46-47 are pending.

Claims 1-3, 10-11, 14, 21, 24, 28, 29, 31-32, 37-40, 42, 46-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species.

Claims 4-9, 12-13, 17-18, 25, and 43, drawn to polynucleotides (DNA) to the extent of SEQ ID NO: 16 are examined on the merits.

The following office action contains NEW GROUNDS of rejection based on the amendment containing new limitations.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 7//7/2008 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Rejections/Objection Withdrawn

The objection of claim 4 and 25 as depending on the non-elected claim 1 is withdrawn in view of the claim 4 and 25 being rewritten as an independent form.

The objection of claim 12 and 18 because the term "a pharmaceutical" recited in the claims is withdrawn in view of the claims being rewritten as "….pharmaceutical composition comprising…."

The objection of specification because it contains an embedded hyperlink is withdrawn in view of the deletion of the embedded hyperlink.

The rejection of Claims 4-9, 12-13, 17-18, 25 and 43 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of the amendment to claims by adding term "an isolated".

The rejections of claims 6 and 7 under U.S.C. 102(b) or 102 (e) as being anticipated by Williams et al., (WO/1999/038972, US Patent, No 6964868) and GeneBank (EST) Accession No. BQ68095 are withdrawn in view of amending the claims to the polynucleotide comprising or consisting of the base sequence represented by SEQ ID NO: 16.

Rejection Maintained and Response to Applicant's Argument:

Rejection under 35 USC § 112 first paragraph:

The following is a quotation of the **first paragraph of 35 U.S.C. 112:**

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement-drawn to pharmaceutical composition comprising antisense of polynucleotide used for therapeutic purpose.

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In this rejection, claims 17 and 18 are interpreted as antisense DNA or RNA complementary to the polynucleotides of SEQ ID NO: 16 having the inhibitory function and being intended use for therapeutic purpose.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to antisense polynucleotide and pharmaceutical composition comprising the antisense to the polynucleotide of SEQ ID NO: 16. The antisense DNA or RNA in the pharmaceutical composition would be intended to be used for the therapeutic purpose to inhibit the expression of the gene product of SEQ ID NO: 16. However, the scope of the instant claims is not commensurate with the enablement of the instant disclosure because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art.

The specification on page 35 teaches that the antisense polynucleotide is generally constituted by bases of about 10 to about 40, preferably about 15 to about 30 and teaches a pharmaceutical composition comprising antisense (page 48+). The specification, examples 2, 3 and 19, teaches a in vitro method of inducting apoptosis of cells, A549 and NCI-H226, by antisense oligonuleotide transfection, and states that TACT427 protein (encoded by SEQ ID NO:16 and its homologies) is disappeared in both cell lines (page 102 line 6+). However, the problems related to therapeutic use of nucleic acids were well known in the art at the time of invention (see for example Agrawal et al. Molecular Medicine Today, 2000, vol. 6, p 72-81), Opalinska et al. (Nature Reviews Drug Discovery, 2002, vol. 1, p. 503-514) and Jen et al. (Stem Cells 2000, vol. 18, p 307-319)). Such problems include the inability to specifically deliver an effective concentration of a nucleic acid to a target cell, such that a target gene is inhibited to a degree necessary to result in a therapeutic effect.

Jen et al. state (see page 313, second column, second paragraph)

"One of the major limitations for the therapeutic use of AS-ODNS and ribozymes is the problem of delivery....presently, some success has been achieved in tissue culture, but efficient delivery for *in vivo* animal studies remains questionable". Jen et al. outlines many of the factors limiting the application of antisense for therapeutic purposes and concludes (see p 315, second column), "Given the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the antisense strategy has proven elusive."

Opalinska et al. state on page 511

"[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA" and in column 2 of the same page, "Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the

> oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded."

Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed pharmaceutical composition *in vivo* in all organisms, with a resultant inhibition of gene expression. The specification provides *examples as set forth above*, however, cell culture examples are generally not predictive of *in vivo* inhibition and the methods of delivery of the exemplified cell line would not be applicable to delivery of oligonucleotides to any organism. Often formulations and techniques for delivery *in vitro* (cell culture) are not applicable *in vivo* (whole organism). For example, Agrawal et al. (see p 79-80, section entitled "Cellular uptake facilitators for *in vitro* studies") states:

> "The cellular uptake of negatively charged oligonucleotides is one of the important factors in determining the efficacy of antisense oligonucleotides.....*In vitro*, cellular uptake of antisense oligonucleotides depends on many factors, including cell type, kinetics of uptake, tissue culture conditions, and chemical nature, length and sequence of the oligonucleotide. Any one of these factors can influence the biological activity of an antisense oligonucleotide."

Due to differences in the physiological conditions of a cell *in vitro* versus *in vivo*, the uptake and biological activity observed *in vitro* would not predictably translate to *in vivo* results. Given these teachings, the skilled artisan would not know *a priori* whether introduction of broadly disclose oligonucleotides *in vivo* by commonly used methodologies of the instant invention, would result in the oligonucleotide reaching the proper cell in a sufficient concentration and remaining for a sufficient time to provide successful inhibition of expression of a target gene. In fact, the state of the art is such that successful delivery of oligonucleotide sequences *in vivo* or *in vitro*, such that the polynucleotide or oligonucleotide provides the requisite biological effect to the target cells/tissues/organs, must be determined empirically.

The specification does not provide the guidance required to overcome the art-recognized unpredictability of using nucleic acids in therapeutic applications in any organism. The teachings of the prior art does not provide that guidance, such that the skilled artisan would be able to practice the claimed therapeutic methods.

Thus, while the specification is enabling for the examples set forth in the specification, the specification is not enabling for the broadly claimed antisense polynucleotide substantially complementary to the polynucleotide of SEQ ID NO: 16 and a pharmaceutical composition for the therapeutic use as the art of inhibiting gene expression by introducing antisense oligonucleotides into an organism is neither routine nor predictable. The amount of experimentation required is such that one of skill in the art could not practice the invention commensurate in scope with the claims without undue, trial and error experimentation and therefore, claims 17 and 18 are not enabled.

Response to Applicant's Argument:

The response filed 7/7/2008 has been carefully considered but is deemed not to be persuasive. On bridging page 11-12 of remarks, Applicants argues:

> the specification provides examples, including working examples, of the use of certain antisense polynucleotides to reduce expression of certain proteins and/or cause apoptosis in cancer cells (see, e.g., Examples 2, 19, 20 and 21).

In response, first, the examples in the specification provides a method using an antisense nucleotide with 20 nucleic acids (SEQ ID NO: 13) for inhibiting the gene expression. The rejection has indicated that the specification is enabling for the examples set forth in the specification (last paragraph of rejection). However, the claimed invention is drawn to an antisense nucleotide with any length and up to 20% of the nucleotide difference from the SEQ ID NO: 16. The specification discloses neither such antisense nucleotides, nor a method of using any antisense located anywhere for the described function. Second, Applicant currently elects polynucleotide of SEQ ID NO: 16 (3072 nts) for examination. The claims are drawn to an antisense having up to 20% of the nucleotide difference from the nucleotides of SEQ ID NO: 16. Disclosed antisense nucleotide of SEQ ID NO: 13 (20 nucleotides) is not elected invention, and

does not belong to the claimed homologues of SEQ ID NO: 16 because the nucleotide of SEQ ID NO: 13 does not count to 80% or more of the SEQ ID NO: 16.

Applicant further provides published references (page 11) showing the use of antisense in the art. This has been also carefully considered but is deemed not to be persuasive. Each antisense inhibitory RNA or DNA has the unique sequence and its function is due to which region of the binding on the DNA or RNA to inhibit the transcription or translation of gene or gene product. One skilled in the art clearly knows that the gene expression is highly regulated in the cells and is not a simple process. Without testing whether designed antisense function either in an in vitro or in vivo model, one skilled in the art could and would not conclude that the antisense nucleotide can perform the function as expected.

Rejection under 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

1. Claims 4-5, 8-9, 12, 13, 17, and 18 remain and are again rejected under 35 U.S.C. 102(b) or 102 (e) as being anticipated by Williams et al., (WO/1999/038972,

published 5/8/1999, 102b or its national stage US Patent, No 6964868, filing March 2000, 102e) as evidenced by DNA database search result reformed as the following:

The rejection cites the pages published in US Patent.

Claim 4 is amended as drawn to a polynucleotide comprising a polynucleotide having at least 80% homology to the polynucleotide of SEQ ID NO: 16.
wherein the polynucleotide is a DNA (claim 5),
Claim 8 and 9 are drawn to a recombinant vector and transformant comprising the polynucleotide of claim 4.
Claims 12, 13 are drawn to a pharmaceutical, diagnostic agent, comprising the polynucleotide
Claims 17-18 are drawn to an antisense complement and a pharmaceutical comprising the antisense or complement to the polynucleotide of SEQ ID NO: 16.

For this rejection, term "a polynucleotide represented by SEQ ID NO: 16" reads on a polynucleotide as small as a few of nucleic acids or any length of a partial polynucleotides of SEQ ID NO: 16.

For this rejection the intended use of a pharmaceutical or diagnostic agent is given no patentable weight.

For this rejection, the antisense polynucleotide recited in claims 17-18 are interpreted as any antisense polynucleotide comprising full or partial DNA or RNA, which is complementary to the polynucleotide of SEQ ID NO: 16.

Williams et al., disclose a polynucleotide with 289 nucleotides (SEQ ID NO: 293), which is a partial sequence of the polynucleotide of SEQ ID NO: 16 with 99.3% local nucleotide identity to the polynucleotide of SERQ ID NO: 16 at position 2620-2889 as evidenced by DNA database search result (attached). Williams et al., disclose a vector and a host cell that carry the nucleotides (col 7 and 10-11, US patent) and also disclose pharmaceutical composition comprising the nucleosides (col 32, 47+, US patent). Williams et al., further disclose antisense nucleotides that are complementary

to the sequence of the SEQ ID NO: 16 and pharmaceutical composition comprising the antisense (col 19 and 47+, US Patent).

Response to Applicant's Argument:

The response filed 7/7/2008 has been carefully considered but is deemed not to be persuasive. On bridging page 12-13 of remarks, Applicants argues:

> The Williams reference does not disclose an isolated polynucleotide comprising a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16, or a polynucleotide consisting of the base sequence represented by SEQ ID NO: 16. The Williams reference also does not disclose vectors, transformants, pharmaceutical compositions, or diagnostic agents as presently claims, nor does Williams disclose an isolated antisense polynucleotide complementary to the base sequence of SEQ ID NO:16 or pharmaceutical compositions thereof. Therefore, the Williams reference does not and cannot anticipate the pending claims.

In response, as stated in the rejection, term "a polynucleotide represented by SEQ ID NO: 16" read on a polynucleotide as small as a few of nucleic acids or any length of a partial polynucleotides represented by SEQ ID NO: 16.

Williams et al., disclose a polynucleotide with 289 nucleotides (SEQ ID NO: 293), which is a partial sequence of the polynucleotide of SEQ ID NO: 16 with 99.3%. Williams et al., also disclose vectors, transformants, pharmaceutical compositions, or diagnostic agents comprising the nucleotides. As such the Williams et al., teach each and every limitation of claims. Applicant is noted that the rejection can be obviated by amending the base claim 4 currently reciting "comprising a polynucleotide represented by SEQ ID NO: 16" to "comprising the polynucleotide of SEQ ID NO: 16" which

containing a polynucleotide longer than or equal to the polynucleotide of SEQ ID NO: 16.

2. Claims 4-5 and 17 remain and are again rejected under 35 U.S.C. 102 (b) as being anticipated by GeneBank (EST) Accession No. BQ68095 submitted April, 2002 as evidenced by Database search result (page 3-4) reformed as the following:

Claims 4-5 and 17 are set forth above.

For this rejection, term "a polynucleotide represented by SEQ ID NO: 16" reads on a polynucleotide as small as a few of nucleic acids or any length of a partial polynucleotides of SEQ ID NO: 16.

The Accession No. BQ68095 discloses a polynucleotide having 973 nucleotides that is 100% local identity to the polynucleotide at position 1-690 of SEQ ID NO: 16 as evidenced by the search result. The polynucleotide of BQ68095 reads on a polynucleotide represented by SEQ ID NO: 16. Since the DNA contain a double strand polynucleotides, which would read on an antisense and complement to the SEQ ID NO: 16.

Response to Applicant's Argument:

The response filed 7/7/2008 has been carefully considered but is deemed not to be persuasive. On page 13 of remarks, Applicants argues:

> The GenBank reference does not disclose an isolated polynucleotide comprising a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16, or a polynucleotide consisting of the base sequence represented by SEQ ID NO: 16. The GenBank reference also does not disclose an isolated antisense polynucleotide complementary to the base sequence of SEQ ID NO:16.

In response, as stated in the rejection, term "a polynucleotide represented by SEQ ID NO: 16" read on a polynucleotide as small as a few of nucleic acids or any length of a partial polynucleotides represented by SEQ ID NO: 16. The Accession No. BQ68095 discloses a polynucleotide having 973 nucleotides that is 100% local identity to the polynucleotide at position 1-690 of SEQ ID NO: 16. The Accession No. BQ68095 teaches each and every limitation of the claims. Applicant is noted that the rejection can be obviated by amending the base claim 4 currently reciting "comprising a polynucleotide represented by SEQ ID NO: 16" to "comprising the polynucleotide of SEQ ID NO: 16" which containing a polynucleotide longer than or equal to the polynucleotide of SEQ ID NO: 16.

Rejection under 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25 and 43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over being anticipated by Williams et al., (WO/1999/038972) in view of Croce et al., (US Patent, 5928884) as the following:

Claims 25 and 43 are drawn to a kit comprising the polynucleotide of SEQ ID NO: 16 or its 80% more homologues.

For this rejection the intended use of a kit is given no patentable weight.

The teaching of Williams et al., is set forth above.

Williams et al., does not teach a kit specifically comprising a polynucleotide of SEQ ID NO: 16.

However, formation of a kit using known component is within the purviews of one skilled in the art. For example, Croce et al., teach diagnostic kit comprising a DNA probe as an active ingredient (col 44, line 32-67).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the polynucleotide of the primary reference by Williams et al., comprising full or partial sequence of SEQ ID NO: 16 in a kit of the secondary reference by Croce et al., with the expected benefit for the screening a compound for the cancer therapy. One of ordinary skill in the art would have been motivated with reasonable expectation of success to use the polynucleotide of Williams et al to the kit of Croce et al., because Williams et al., have shown partial polynucleotide and Croce et al., have shown a method of making a kit.

Response to Applicant's Argument:

The response filed 7/7/2008 has been carefully considered but is deemed not to be persuasive. On page 14 of remarks, Applicants argues:

> the William reference cannot render obvious claims 25 and 43 (and the Office Action does not suggest otherwise). Applicants contend that the Croce reference - which also does not disclose a polynucleotide represented by SEQ ID NO:16, or a polynucleotide having at least 80% homology to the polynucleotide represented by SEQ ID NO:16 - cannot "bridge the gap" between the teachings of the Williams reference and the subject matter of the pending claims.

In response, the rejection is based on the guideline of MPEP 2141:

"in determining the difference between the prior art and the claims, the question under 35 USC103 is not whether the difference themselves would have been obvious, but whether the claimed invention as a whole would have been obvious" .

William reference teaches the nucleotides in the claimed kit. Making a kit for the purpose of detecting the gene expression is within the purviews of one skilled in the art and would be obvious for any skilled molecule and cellular biologist. The skilled artisan would be motivated with high expectation of success to put the polynucleotide of SEQ ID NO:16 and its homologues in the kit. Thus, Applicant's argument has not been found persuasive, and the rejection is maintained.

The following is a New Ground of rejection-based on the amendment

Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 5, 8, 9, 12, 13, 17, 18, 25, 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotides of SEQ IDN O:16 and the vector , the transformant, the pharmaceutical composition , and the diagnosing kit comprising the polynucleotides of SEQ IDN O:16, does not reasonably provide enablement for its variant having at least 80% homology to the polynucleotide of SEQ ID NO: 16, The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to

practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims are broadly drawn to polynucleotides comprising a (any) polynucleotide SEQ ID NO: 16 or a (any) polynucleotide having at least 80% homology to the polynucleotide of SEQ ID NO: 16. Thus, the claims are inclusive of a genus of polynucleotides having less than 20% of the nucleic acid mutation, deletion, addition of SEQ ID NO: 16 at anywhere and with any length. To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The specification first teaches that the differential expression of the gene FLJ20539 (Genbank accession No: AK000546) is found in human gastric cancer and other human cancers (page 1, and example 1). Using the primer from the gene FLJ20539, the high homologous TACT427-A cDNA (SEQ ID NO: 16) is cloned from human brain cDNA library (example 4). The specification then teaches that the enhanced expressions of both FLJ20539 and TACT427A genes are found in many cancer tissues and cell lines (example 1 and examples 8+). The specification although discloses a few homologous clones of TACT427-A (SEQ ID NO: 16, 3072 nts) having longer (ID NO: 19, 3505 nts) or short nucleotide sequence (SEQ ID NO: 18, 3060 nts), the specification does not teach the substitutions, mutations,

deletions, additions anywhere up to 20% of the nucleic acids of SEQ ID NO: 16, which are differentially expressed in cancer cells or tissues. As such, one skilled in the art would not know how to make and use the claimed variants of SEQ ID NO: 16 comprising detecting the expression in a tumor for either diagnosis or treating a tumor condition.

The sequence of SEQ ID NO: 16 (3072 nts) is free of the art, however the protein with high sequence identical the partial or even entire sequence of SEQ ID NO: 16 are comprised in the known proteins. The differential expressions of such homologous are not necessarily involved in the cancer conation. For example, Brlouchi et al., (WO2006116867-SEQ ID NO: 546, 3520 ntds) teach a Crohns disease related polynucleotide having more than 90% sequence identity to the polynucleotides of SEQ ID NO: 16. Brlouchi et al., teach that the expression of the gene is indicative susceptibility to Crohn's diseases (see attached search result). As such, skilled artisans have recognized that the expression of the homologous of the nucleotides of SEQ ID NO: 16 may be involved in more than a cancer conditions. The relationship between these abnormal conditions and expression of the nucleotide of SEQ ID NO: 16 or variant thereof are not predictable and undue experimentations must be required for one skilled in the art to make and use of the nucleotides of SEQ ID NO: 16 in any of those conditions.

Reasonable correlation must exist between the scope of the claims and scope of enablement set fort. The specification dose not provide objective evidence for claimed homologous at least 80% to TACT427-A (SEQ ID NO: 16) as what has been disclosed

for the function and expression of TACT427-A (SEQ ID NO: 16. Thus, in view of the lack of predictability of the prior art, the breadth of the claims, the lack of guidance and support in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

Claim Objection

Claim 6 is objected to as being dependent upon the rejected claims 5, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claim 7 is free of art and allowed.

Claims 4-6, 8-9, 12-13, 17-18, 25, and 43 are objected or rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643